Mod Rheumatol (2008) 18:193–199
DOI 10.1007/s10165-008-0027-2

CASE REPORT

Therapeutic efficacy of intravenous cyclophosphamide concomitant with moderate- to high-dose prednisolone in two patients with fasciitis panniculitis syndrome

Takashi Kato · Ayako Nakajima · Makoto Soejima · Reon Nagai · Toru Yago · Kiyoko Tanohara · Hisae Ichida · Ikuko Masuda · Toru Yamada · Atsuo Taniguchi · Yuji Akiyama · Toshihide Mimura · Tetsuya Tsuchida · Naoyuki Kamatani · Masako Hara

Received: 5 July 2007 / Accepted: 31 October 2007 / Published online: 20 February 2008

Abstract Fasciitis panniculitis syndrome (FPS) has been proposed as a new category of 'fasciitis' and includes the well-established eosinophilic fasciitis (EF). Unlike EF, FPS exhibits inconsistent eosinophilia and/or eosinophilic infiltration of the lesions. Principal histological FPS findings include dermal thickening, inflammation and thickening of the subcutaneous fat tissue, fibrous thickening of the fascia and inflammation of the adjacent muscle. FPS is commonly resistant to corticosteroids, and cimetidine is effective in approximately 80% of FPS patients. A new therapy for FPS is required for cases refractory to treatment or intolerant to cimetidine because of adverse drug reaction. In this report, two FPS patients were resistant to corticosteroids. Both received intravenous cyclophosphamide (IVCY) concomitant with moderate- to high-dose prednisolone (PSL), and this effectively treated the induration of the FPS lesions. Patient 1 was a 50-year-old woman who had been diagnosed with fasciitis following *en bloc* muscle biopsy of the thigh. She had been treated with high-dose PSL for 6 years, but the fasciitis was refractory. Induration of the neck, thorax and thighs resulted in impaired neck rotation, restrictive respiratory failure and impaired walking. A diagnosis of FPS was made by re-assessing the *en bloc* muscle biopsy. Although PSL (40 mg/day) for 18 days was ineffective, the addition of IVCY (400 mg) dramatically improved the disease manifestations. Patient 2 was a 68-year-old man who was diagnosed with fasciitis based on *en bloc* muscle biopsy of the left foot. He had been treated with PSL for 16 years, but the fasciitis was refractory. He exhibited lower limb induration and a refractory skin ulcer of the left foot. A diagnosis of FPS was made by re-assessing the *en bloc* muscle biopsy. Although PSL (40 mg/day) for 2 weeks was ineffective, the addition of IVCY (450 mg) improved both the lower limb induration and the skin ulcer. FPS may cause both entrapment vasculopathy of subcutis and perivasculitis of the subcutaneous fat tissue such that the skin ulcer might be closely related with the ischemic mechanism triggered by FPS. According to the clinical courses of our cases, IVCY combined with moderate- to high-dose PSL may be a new therapeutic choice for corticosteroid-resistant FPS patients.

Keywords Eosinophilic fasciitis (EF) · Fasciitis panniculitis syndrome (FPS) · Intravenous cyclophosphamide (IVCY) · Restrictive respiratory failure · Systemic sclerosis

T. Kato · A. Nakajima · M. Soejima · R. Nagai · T. Yago · K. Tanohara · H. Ichida · I. Masuda · T. Yamada · A. Taniguchi · N. Kamatani · M. Hara
Institute of Rheumatology, Aoyama Hospital, Tokyo Women's Medical University, 2-7-13 Kitaaoyama, Minato-ku, Tokyo 107-0061, Japan

Y. Akiyama · T. Mimura
Department of Rheumatology, Saitama Medical University, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan

T. Tsuchida
Department of Dermatology, Saitama Medical University, 38 Morohongo, Moroyama-machi, Iruma-gun, Saitama 350-0495, Japan

T. Kato (✉)
Institute of Rheumatology, Tokyo Women's Medical University, 10-20 Kawada-cho, Shinjuku-ku, Tokyo 162-0054, Japan
e-mail: kintarou@s9.dion.ne.jp

Introduction

In 1990, Naschitz et al. proposed fasciitis panniculitis syndrome (FPS) as a new category of fasciitis, including

well-established categories of fasciits such as eosinophilic fasciitis (EF) [1, 2]. EF was described originally by Shulman in 1975 as a scleroderma-like disorder characterized by inflammation and fibrous thickening of the subcutis and deep fascia with peripheral eosinophilia and/or eosinophilic infiltration of the subcutis and fascia [3]. On the other hand, the concept of FPS is inconsistently associated with a peripheral eosinophilia and eosinophilic infiltration of the lesions [4]. In addition to EF, FPS includes several conditions with histological pictures similar to EF, containing morphea profundus, lupus profundus, graft-versus-host reaction, cancer-associated fasciitis and infection, such as brucellosis associated fasciitis [4]. The histological findings consist of dermal thickening, inflammation and fibrous thickening of the subcutaneous fat tissue, fibrous thickening of the fascia and inflammation of the adjacent muscle [4, 5]. The histological findings are essential to FPS, and the FPS lesions cause induration of the extremities and trunk. As a result of the induration, FPS patients can suffer from disturbance of walking and thoracic movement [4, 6]. Although treatment with corticosteroids is usually effective for EF [3], the majority of FPS patients are corticosteroid resistant [2, 4]. On the other hand, some patients with FPS, such as infection-associated FPS, may exhibit spontaneous resolution [4]. Furthermore, cancer-associated FPS patients can also remit spontaneously after successful resection of the tumor [7, 8]. Naschitz et al. reported that treatment with cimetidine was effective in around 80% of FPS patients [1, 2, 4]. However, new therapeutic approaches are required for FPS patients who are refractory to cimetidine or intolerant to cimetidine because of adverse drug reaction.

In this report, we described two cases with corticosteroid-resistant FPS who were dramatically improved by treatment with intravenous cyclophosphamide (IVCY) concomitant with prednisolone (PSL). To our knowledge, efficacy of IVCY in patients with FPS has not been reported. IVCY may represent a novel therapeutic modality for patients with corticosteroid-resistant FPS.

Case reports

Case 1

Patient 1 was a 50-year-old Japanese woman who had suffered from fasciitis affecting the bilateral thighs for 6 years. She was admitted to our hospital in August 2006 because of recent worsening induration of the neck, trunk and thighs. She had become unable to walk independently and became wheelchair dependent. In addition, she was unable to rotate her neck fully, and the range of motion was severely limited (almost zero degree). The patient was sent to our institute for a second opinion regarding diagnosis and treatment. A diagnosis of fasciitis was made in 2000 following an *en bloc* muscle biopsy from the right thigh. Treatment with high-dose PSL, such as 60 mg daily for 7 weeks, and methotrexate (6 mg/week) had been undertaken, but had resulted in a poor therapeutic result. The only significant past medical history was hypertension. On admission, her height and weight were 150 cm and 33.6 kg, respectively. She was afebrile and hypertensive (187/65 mmHg) with a regular pulse rate (60 per min). Subcutaneous induration of the dorsal thorax, both thighs and sternocleidomastoid muscles was evident (Fig. 1). The skin was not sclerotic, and pinching the skin was intact except over the chest and abdomen. The manual muscle test revealed impaired strength of neck flexion (2/5) and mild weakness of the extremities (4/5). The respiratory movement of the thorax was also impaired by induration of the chest with a reduced circumferential difference between inspiration and expiration of 1.5 cm (normal range >2.5 cm). Myalgia and arthralgia were absent with no ankyloglossia, sclerodactyly, Raynaud's phenomenon or nail fold thrombi. The laboratory findings demonstrated a normal circulating white blood cell count (7,800/μl) without any eosinophila, and the erythrocyte sedimentation rate (ESR) was 14 mm/h. Blood chemistry showed slight elevation of the levels of myogenic enzymes and proteins: creatine phosphokinase (CK), 433 U/l (normal range, 40–150); CK-MB, 13.9 ng/ml (normal range, <5.2); aldolase, 8.6 U/l (normal range, 2.7–5.9); myoglobin

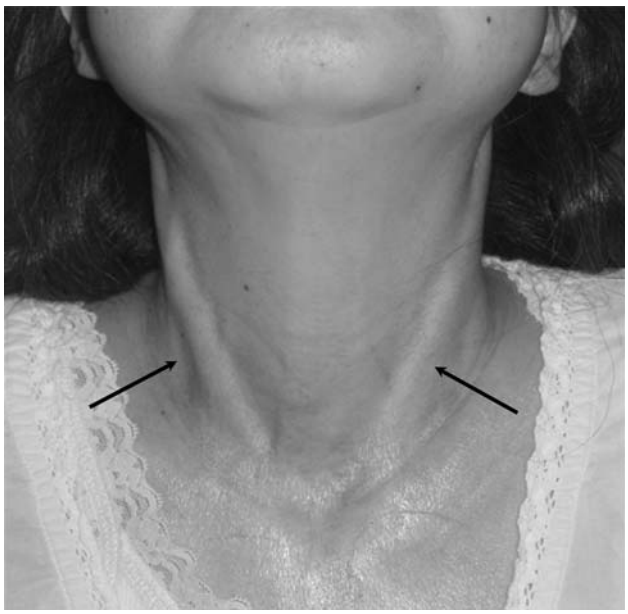

Fig. 1 Protrusion of the sternocleidomastoid muscles in case 1. *Arrows* indicate the protruding sternocleidomastoideus, which may be caused by decreased mobility of the subcutis and the fascia of the muscles. The skin on the anterior chest appears sclerotic with brightness

138 ng/ml (normal range, <60). In addition, C-reactive protein (CRP) was not elevated, complement levels were normal, and anti-nuclear antibody (ANA) levels were within normal limits. Thyroid function was normal. Blood gas analysis (BGA) obtained on room air was as follows; pH 7.395, pCO_2 54.1 mmHg, pO_2 93.8 mmHg, and HCO_3 32.4 mmol/l, which were compatible with a respiratory acidosis. The chest X-ray showed an intact lung field and normal movement of the diaphragm between inspiration and expiration. Respiratory function tests revealed an extremely reduced vital capacity (41.1% of the predicted value) with a normal forced expiratory rate (97.06% of the predicted value). These findings were consistent with respiratory failure caused by disturbed and restricted thoracic movement. An electromyogram revealed a myogenic pattern of the proximal extremities. Gallium scintigraphy demonstrated bilateral accumulation of tracer in the thighs. Magnetic resonance imaging (MRI) of the thighs demonstrated enhancement of the fascia of the thighs that was compatible with a diagnosis of fasciitis (Fig. 2). In addition, enhancement of the adjacent muscle to the fascia was partially observed (Fig. 2). The *en bloc* muscle biopsy obtained from the right thigh in 2000 was re-assessed, and thickening of the dermis, inflammation and thickening of the septum of the subcutaneous fat tissue, fibrous thickening of the fascia and mild inflammation of the muscle near the fascia were noted, while eosinophilic infiltration was not evident (Fig. 3a–d). In the light of these findings, a diagnosis of FPS was made [4]. The restrictive respiratory failure was considered to result from severe induration of the thorax secondary to FPS. Skin biopsy of the abdomen was performed on day 10, and the findings demonstrated fibrous thickening of the dermis, accumulation of excess collagen fibers and a reduced number and size of the dermal appendages compatible with systemic sclerosis (Fig. 3e). Various investigations for malignancy were negative. Treatment with 40 mg of PSL daily for FPS began on hospital day 6; however, despite this treatment, her ability to walk only slightly improved, and she remained significantly disabled (Fig. 4). Then, intravenous cyclophosphamide (IVCY, 400 mg) was administered on day 23. Three weeks after commencing IVCY, her disabilities rapidly improved, and she was able to walk well with a stick (Fig. 4). In addition, the subcutaneous induration of the neck improved, and she was able to rotate her neck almost normally (Fig. 4). Furthermore, the vital capacity increased from 41.1 to 54.7% of the predicted value on day 46 (Fig. 4). This was associated with an improvement in the pCO_2 level that fell from 54.1 to 45.2 mmHg on day 47 (Fig. 4). She was commenced on 400 mg of cimetidine daily on day 50 [1, 4, 6]. A second treatment of IVCY (400 mg) was performed on day 57, and she was discharged from the hospital on day 70. By 9 months after discharge, three additional doses of IVCYs (400 mg) had been administered as maintenance treatment, and her symptoms of impaired walking, reduced neck rotation and restrictive respiratory failure had almost normalized.

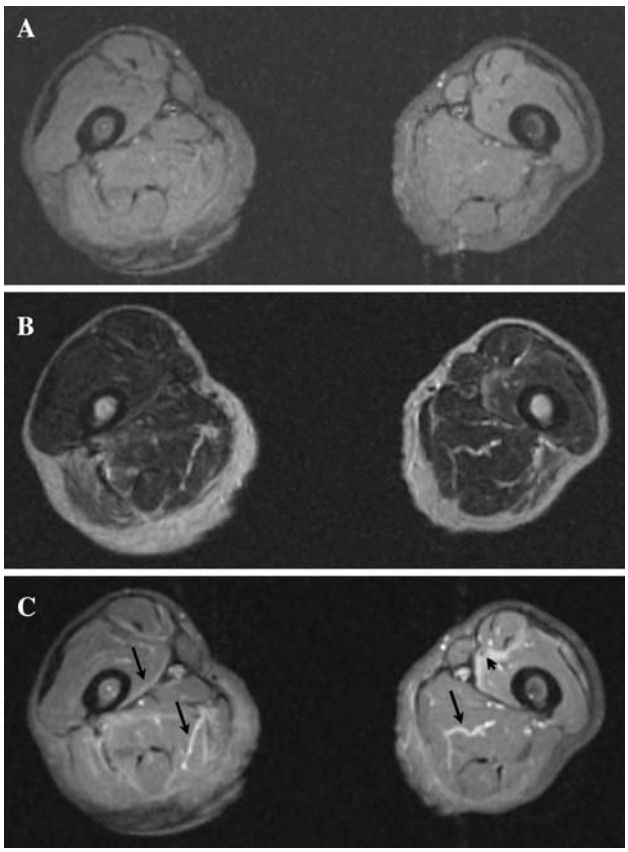

Fig. 2 Thigh MRI in case 1 performed on day 3. **a**, **b** and **c** are T1-weighted, T2-weighted and gadolinium-enhanced T1-weighted axial images, respectively. In **c**, *arrows* depict contrast enhancement along the fascia, which is consistent with fasciitis. In **c**, the *arrowhead* shows contrast enhancement of not only the fascia, but also the muscle adjacent to the fascia. These findings are compatible with FPS

Case 2

Patient 2 was a 68-year-old Japanese man suffering from fasciitis of the lower limbs for 16 years. He was admitted to our hospital in September 2006 because of a skin ulcer on the left foot. A diagnosis of fasciitis was made in 1994 following an *en bloc* muscle biopsy of the left lower limb. Treatment with PSL, such as 30 mg daily for 3 weeks, combined with disease-modifying anti-rheumatic drugs (DMARDs), such as bucillamine and D-penicillamine, had been ineffective, and a skin ulcer of the left foot had developed and been present for 6 months. He had a past medical history of hypertension and was allergic to H2 blockers (famotidine), which had not been prescribed. On admission, his height and weight were 165.4 cm and 57 kg,

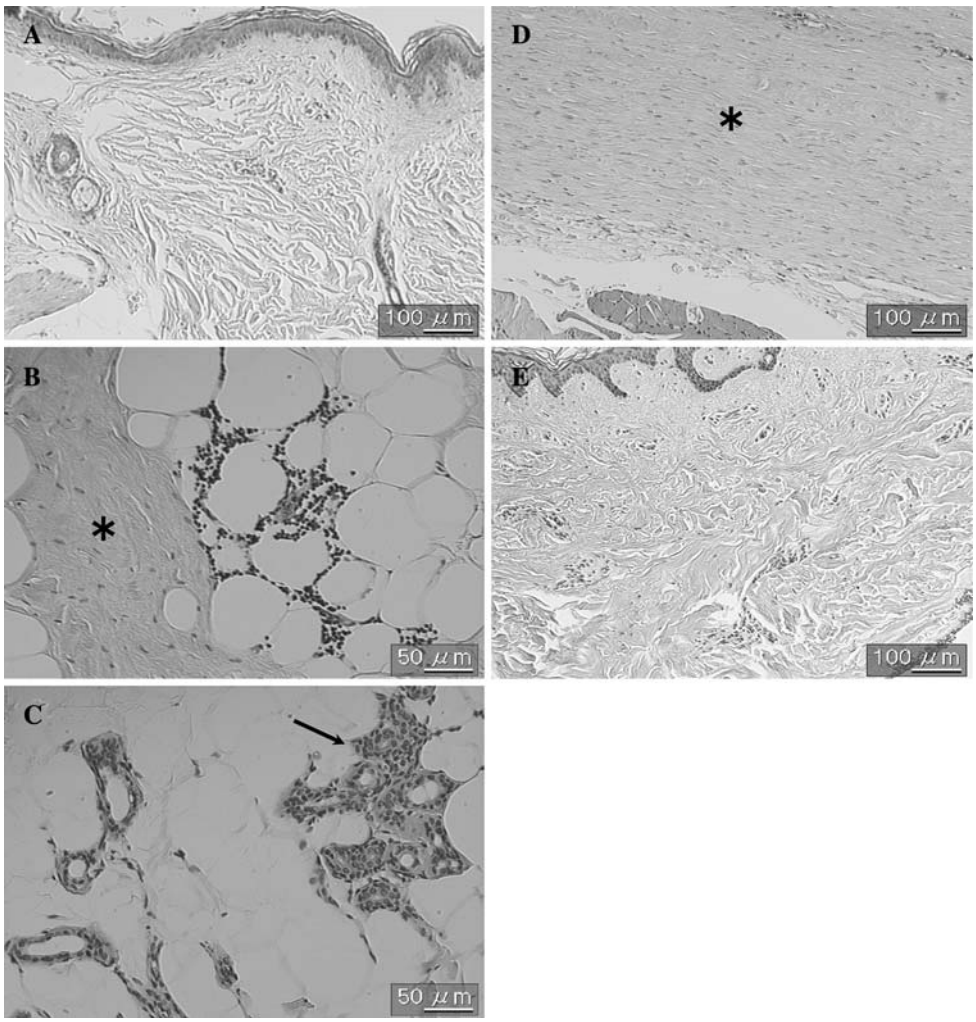

Fig. 3 **a**, **b**, **c** and **d** are findings of the *en bloc* muscle biopsy from the right thigh of patient 1 performed in 2000. **a** shows thickening of the dermis; **b** demonstrates lymphocytic inflammation and thickening of the septum of the subcutaneous fat tissue. *Asterisk* indicates the thickened septum. **c** shows perivasculitis (*arrow*) of the septum of the subcutaneous fat tissue; **d** demonstrates fibrous thickening of the fascia (*asterisk*). Eosinophilic infiltration is not observed in **a**, **b**, **c** and **d**. **e** depicts findings of the abdominal skin biopsy performed on day 10 of the current admission in case 1. Fibrous thickening of the dermis with marked deposition of collagen fibers and decreasing number and size of the dermal appendages are shown. Scale bars are 100, 50, 50, 100 and 100 μm on **a**, **b**, **c**, **d** and **e**, respectively

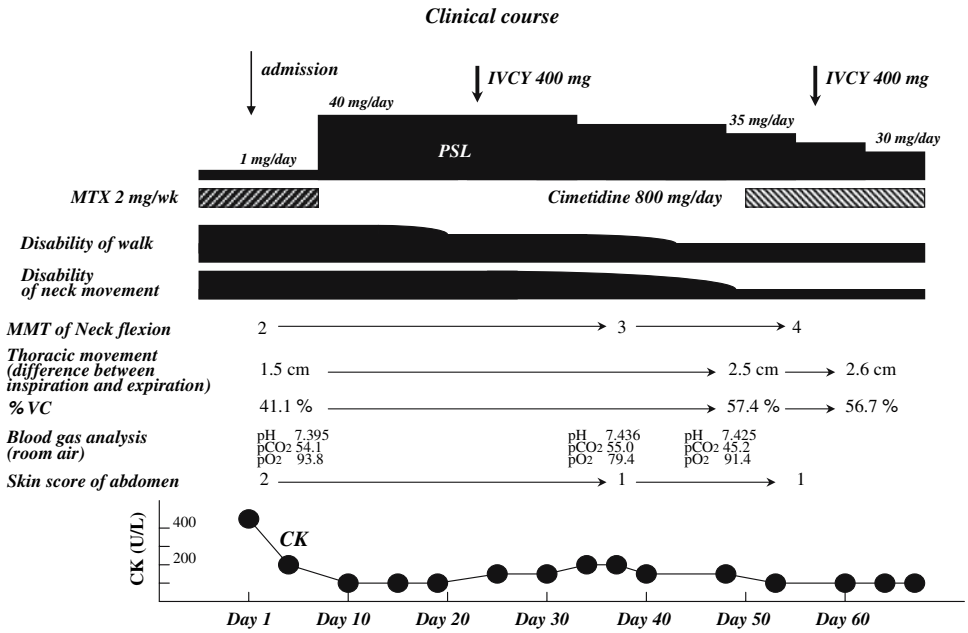

Fig. 4 Clinical course of case 1. Abbreviations: *CK* creatinine kinase, *IVCY* intravenous cyclophosphamide, *MMT* manual muscle test, *MTX* methotrexate, *PSL* prednisolone, *VC* vital capacity

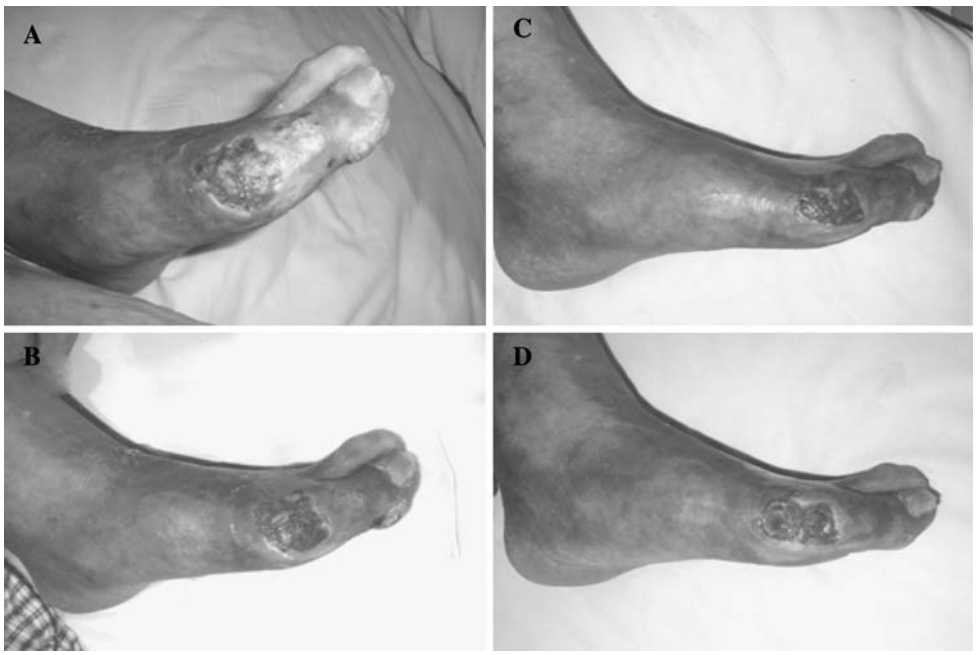

Fig. 5 Serial photographs of the skin ulcer of the left foot in patient 2. **a** was taken before starting treatment with 40 mg of PSL daily. A skin ulcer with diameter of 3.5 cm is shown; **b** was taken on day 23 (11 days after starting treatment with 40 mg of PSL daily), and the ulcer size has not decreased in comparison with **a**; **c** was taken on day 46 (22 days after the first IVCY), and the ulcer size appears smaller than that of **b**. **d** was taken on day 62 (12 days after the second IVCY). The ulcer size is much smaller than that of **c**, and the diameter is approximately 2.5 cm

respectively. He was afebrile and slightly hypertensive (149/92 mmHg) with a regular pulse (74 per min). Physical findings included induration of the lower limbs (the crura and the feet) and a skin ulcer of the left foot (diameter 3.5 cm) (Fig. 5a). The skin color of the affected area was dark brown. Sclerosis of the lesions was apparent, and pinching the skin of the lesions was impossible. In addition, mobility of the subcutaneous area was also abnormal. Pulsation of the left dorsal foot artery was extremely weak, and neuralgic pain of the left foot was observed. There was no evidence of Raynaud's phenomenon, nail fold thrombi or coldness of the skin of the distal extremities. No other abnormal physical findings were evident.

The laboratory findings revealed an elevated white blood cell count (12,200/μl) with no eosinophilia and an elevated ESR (90 mm/h). Blood chemistry, including the CK and aldolase levels, were normal except for slightly elevated HbA1c (6.8%). The CRP level was increased (5.79 mg/dl), and the rheumatoid factor was positive (33 IU/ml). Other autoantibodies, including ANA, anti-neutrophil cytoplasmic antibodies (ANCA) and anti-cardiolipin beta 2-glycoprotein I complex antibody, were not detected, and lupus anti-coagulant was negative, while the other laboratory findings were normal. Lower limb ultrasonography revealed no evidence of deep-vein thrombosis, while lower limb three-dimensional computed-tomographic scanning angiography (3D-CTA), capable of detecting arterial lesions from the popliteal artery to the dorsal foot artery, did not demonstrate any occlusive arterial lesions. The findings of the *en bloc* biopsy of the left lower limb performed in 1994 were re-assessed, and the following features were detected: dermal thickening, inflammation and thickening of the septum of the subcutaneous fat tissue and fibrous thickening of the fascia in the absence of eosinophilic infiltration. Several investigations for malignancy were negative. In the light of these findings, a diagnosis of FPS concomitant with a skin ulcer was made [4]. On day 12, treatment with 40 mg of PSL daily was commenced, and the CRP level decreased to 0.19 mg/dl 10 days later. The crus MRI was performed on day 21 and demonstrated contrast enhancement along the fascia of the tibialis anterior, extensor digitorum longus and soleus (Fig. 6c). These findings were consistent with the diagnosis of FPS. Despite treatment with PSL (40 mg/day) for 2 weeks, the size of the skin ulcer of the left foot did not decrease, and IVCY (450 mg) was administered on day 26 (Fig. 5b). The ulcer size became smaller 2 weeks after IVCY, and the color of the lower limbs significantly improved. In addition, induration of the subcutaneous tissue of the lower limbs began to lessen. PSL at a dose of 40 mg daily was given for 2 weeks, and the dosage was tapered thereafter. The size of skin ulcer of the left foot became smaller still by 30 days after the first IVCY (Fig. 5c). On day 53, the second IVCY (450 mg) was administered, and the skin ulcer of the left foot reduced further in size; the diameter decreased to 2.5 cm on day 53 (Fig. 5d). By day 55, the neuralgic pain affecting the left foot became markedly worse, and daily treatment with carbamazepine (200 mg) was commenced. The neuralgic pain resolved partially with the treatment. The patient was discharged from the hospital on day 64. Topical treatment with trafermin (recombinant basic fibroblast growth factor) had been concomitantly performed for the skin ulcer since the onset. The skin ulcer of the left foot had healed by

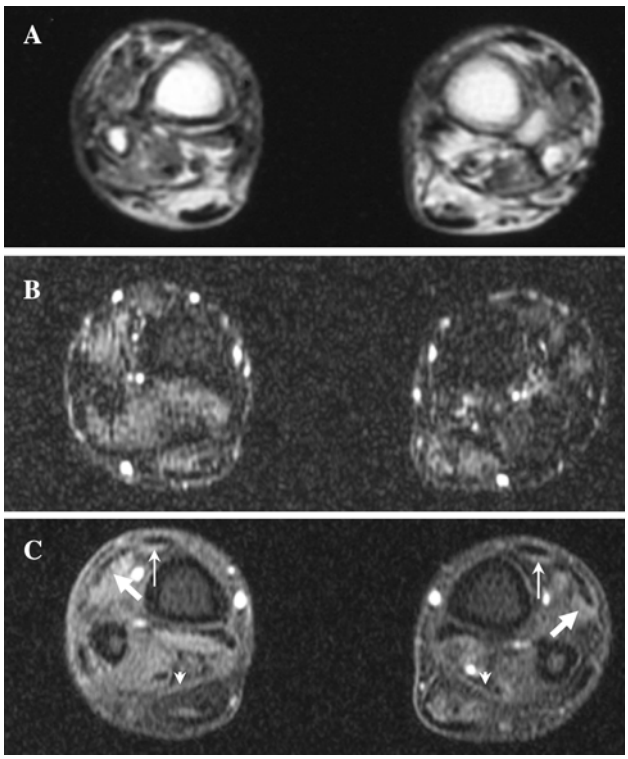

Fig. 6 Crus MRI in case 2 performed on day 21. **a**, **b** and **c** are T1-weighted, T2-weighted (fat suppression) and gadolinium-enhanced T1-weighted (fat suppression) axial images, respectively. In **c**, *thin arrows* indicate contrast enhancement along the fascia of the tibialis anterior. *Thick arrows* demonstrate contrast enhancement along the fascia of extensor digitorum longus. *Arrowheads* depict contrast enhancement along the fascia of soleus. The enhancement is apparent in comparison with **a**

5 months following discharge without any additional treatment with IVCY.

Discussion

Both cases in this report had been diagnosed with 'fasciitis' initially, and treatment mainly with PSL had been commenced like EF; however, both patients were resistant to the treatment. Recently, FPS was proposed as a new category of 'fasciitis.' The two cases described in this report were fully consistent with pathological and clinical characteristics of FPS. In particular, our patients were corticosteroid resistant because the manifestations of FPS had not improved satisfactorily during the treatment with PSL for about 2 weeks. Therefore, another therapeutic choice was necessary to add to the effect of treatment with corticosteroids alone.

Therapeutic efficacy of cimetidine for FPS has previously been reported [1, 4, 6], but the mechanism is unclear. In our cases, the therapeutic efficacy of combination treatment with IVCY and moderate- to high-dose PSL was assessed without administration of treatment with H2 blockers, such as cimetidine. In patient 1, the first course of IVCY was performed before treatment with H2 blocker, while patient 2 did not receive a H2 blocker because of a history of previous drug allergy to famotidine (one of the H2 blockers). Therefore, the therapeutic efficacy of combined treatment with IVCY and PSL for FPS was demonstrated in both cases without the potentially confounding contributing influences of H2 blockers, such as cimetidine.

Efficacy of moderate- to high-dose PSL for FPS in our cases was considered unsatisfactory, and thus IVCYs were performed subsequently. Furthermore, the clinical courses before the current admission also suggested that both FPS patients were resistant to PSL. However, partial improvement by treatment with PSL was also observed in both patients before IVCYs during the current admission. In addition, therapeutic efficacy of the first IVCY began to take place a few days after the start of IVCY, which is too early to detect its efficacy, because therapeutic efficacy of IVCY for rheumatic diseases is usually observed 10 to 14 days after treatment [9]. The improvement observed within a few days after IVCY in patient 1 also might be related to mild efficacy of high-dose PSL for FPS in patient 1.

In patient 1, the neck and thorax were also severely involved by FPS lesions that resulted in impaired neck rotation and restrictive respiratory failure, respectively. In EF itself, the lesions commonly affect the extremities, with truncal lesions being uncommon [3]. Uehara et al. demonstrated that the cervicothoracic lesions of FPS may finally result in respiratory arrest concomitant with CO_2 narcosis, necessitating intubation [10]. Kishi et al. also reported a case of FPS whose thoracic movement was disturbed by induration of the chest due to FPS lesions [6]. Thus, truncal induration and the resultant sequelae are serious manifestations of FPS, and therapeutic intervention with cimetidine and/or IVCY should be considered.

In patient 2, the refractory skin ulcer occurred on the thickened FPS lesion. Before the current admission, the skin ulcer of the left foot had worsened gradually in spite of topical treatment with trafermin (recombinant basic fibroblast growth factor). Treatment with IVCY concomitant with PSL did, however, improve both the induration of the lower limbs (the crura and the feet) and the skin ulcer on the foot. The clinical course suggests that the skin ulcer was closely related to the FPS. An entrapment vasculopathy can take place in FPS because the microcirculation for the skin exists between the subcutis and the subcutaneous fat tissue. Furthermore, a perivasculitis can be observed in the affected septum of the subcutaneous fat tissue in FPS [4, 8]. As a result of these histological features, formation of skin ulcers in FPS may be closely related to ischemic changes resulting from entrapment vasculopathy and

perivasculitis associated with FPS. These considerations are consistent with the 3D-CTA findings in patient 2 who did not demonstrate any obstructive arterial lesions from the popliteal to the dorsal foot arteries, i.e., the 3D-CTA findings support the consideration that the skin ulcer of the left foot was caused by disturbance of the microcirculation due to FPS. However, histological investigation of the skin ulcer in patient 2 had not been performed during the current admission, so the precise pathogenesis of the skin ulcer is still a matter of speculation. In addition, the left foot was also affected by neuralgic pain. The peripheral nerve system of the skin also passes through the subcutis and subcutaneous fat tissue and may therefore be affected by the entrapment neuropathy that may be evident in FPS.

Neither case in this report was associated with malignancy. Naschitz et al. demonstrated that 3 of 32 FPS cases were associated with malignancy [4]. Malignancy-associated FPS requires treatment for the malignancy in order to improve panniculitis and fasciitis. Furthermore, some patients with cancer-associated FPS can spontaneously remit after successful cancer resection [8]. In addition, the efficacy of treatment with cimetidine might be inferior to that of cancer-unrelated FPS [4]. Therefore, it is important to clarify whether the FPS is associated with malignancy in order to choose an effective treatment for FPS.

In summary, treatment with IVCY coupled with moderate- to high-dose PSL may be effective in patients with corticosteroid-resistant FPS. IVCY may be a new therapeutic choice for corticosteroid-resistant FPS patients.

Conflict of interest There were no conflicts of interests among the co-authors of this case report for publication in the journal.

References

1. Naschitz JE, Yeshurun D, Rosner I, Abrahamson JE, Misselevitch I, Boss JH. Treatment with cimetidine of atypical fasciitis panniculitis syndrome. Ann Rheum Dis. 1990;49:788–92.
2. Naschitz JE, Yeshurun D, Zuckerman F, Rosner I, Shairawi I, Missellevitch I, et al. The fasciitis-panniculitis syndrome: clinical spectrum and response to cimetidine. Semin Arthritis Rheum. 1992;21:211–20.
3. Seibold JR. Scleroderma. In: Harris Jr ED, Budd RC, Firestein GS, Genovese MC, Sergent JS, Ruddy S, Sledge CB, editors. Kelley's textbook of rheumatology (7th ed). Philadelphia: Elsevier, 2005. pp. 1279–308.
4. Naschitz JE, Jochanan H, Misselevich I, Yeshurun D, Rosner I. The fasciitis-panniculitis syndrome: clinical and pathologic features. Medicine. 1996;75:6–16.
5. Morales M, Dias J, Oueiroz A, Santiago M. Fasciitis-paniculitis syndrome simulating deep venous thrombosis. Eur J Intern Med. 2007;18:244–5.
6. Kishi T, Yamamoto Y, Furukawa F. Case of fasciitis panniculitis syndrome. J Dermatol. 2007;34:92–4.
7. Naschitz JE, Yeshurum D, Zuckerman F, Rosenbaum M, Misselevitch I, Shairawi I, et al. Cancer-associated fasciitis panniculitis. Cancer. 1994;73:231–5.
8. Ido T, Kiyohara Y, Sawai T, Kumakiri M, Ishiguro K. Fasciitis-panniculitis syndrome and advanced gastric adenocarcinoma in association with antibodies to single-stranded DNA. Br J Dermatol. 2006;155:640–1.
9. Haga HJ, D'Cruz D, Asherson R, Hughes GR. Short term effects of intravenous pulses of cyclophosphamide in the treatment of connective tissue disease crisis. Ann Rheum Dis. 1992;51:885–8.
10. Uehara R, Suzuki Y, Asanuma Y, Ichikawa Y, Abe M. Ventilatory failure due to the limitation of chest movement in a case of FPS. Nihon Rinsho Meneki Gakkai Kaishi. 2001;24:36–42 (in Japanese).